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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MILLER, MARINA I	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,052	BERLIN ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-50* is/are rejected.

7)☒ Claim(s) *2-13,15-27,29-39 and 41-50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of species of cancer in the reply filed 11/13/2006 is acknowledged.

Claims 1-50 are pending.

An action on the merits of claims 1-40, as they read on the elected species, follows.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed 2/6/2004 has been considered in full.

Claim Objections

Claims 2-13, 15-27, 29-39, and 41-50 are objected to because of the following informalities: claims 2-13, 15-27, 29-39, and 41-50 are dependent claims and depend from claims 1, 14, 28, and 40, respectively. The dependent claims should begin by reciting "[t]he method", [t]he system", or '[t]he computer program according to claim" 1, 14, 28, or 40. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13, 28-30, and 32-39 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 is directed to a method for guiding selection of a therapeutic treatment regimen comprising steps of providing information about methylation of DNA of a patient and generating a ranked list of diseases based on the methylation and knowledge base based on expert rules for evaluating and selecting a type of disease based on methylation status of DNA of a patient. The dependent claims further recite steps of generating, *in the computing device,* advisory information and accessing information via the computer device. Dependent claim 7 recites that patient information includes prior information stored in a computer device. However, not all processes are statutory under 35 U.S.C. 101. *See* MPEP 2106 (Section IV in particular). To satisfy 101 requirements, the claim must be for a practical application, which can be met if the claimed invention "transforms" an article or physical object to a different state or thing OR the claimed invention otherwise produces a useful, concrete, and tangible result. If claims are directed to abstract ideas (such as mathematical algorithms), natural phenomena, and laws of nature, the claims must be considered as a whole for determining whether an abstract ideas, natural phenomena, or laws of nature has a particular application.

In the instant case, the claimed method steps describe nothing more than the manipulation of basic mathematical constructs, the paradigmatic 'abstract idea.' MPEP 2106 Section IV. Specifically, the claimed method recites mathematical and/or statistical manipulations with methylation information. The claimed method does not transform or reduce an article or a physical object (*e.g.*, methylated DNA) to a different stage or thing because the "result" of the method (*i.e.*, generated rakned list of diseases; ranked therapeutic treatment regiments, advisory information) is merely data (information) and is not equivalent to physical transformation. The claims do not recite tangible expression (*i.e.*, real-world result) of generated ranking or advisory

information, nor any recitation of an actual (*i.e.*, concrete) result in a form useful to one skilled in the art. Thus, the method does not recite steps of producing something that is concrete, useful, and tangible, and is not statutory.

Claims 28-30, and 32-39 recite an apparatus' components by referring to function/structure. "35 U.S.C. 112, sixth paragraph states that a claim limitation expressed in means-plus-function language 'shall be construed to cover the corresponding structure ... described in the specification and equivalents thereof.'" See MPEP 2181. The specification discloses a computer system comprising a program for performing steps of the instant method (p. 28-31). Therefore, means for providing information about the methylation status and means for generating a ranked listing and advisory information are interpreted to be a program for performing the instant steps. Further, the instant system comprises "a computing device" comprising a first and second knowledge base. It is not obvious what structural components of "a computing device" are specifically required by the claims because a "knowledge base" may be a program or a database recorded on paper (*i.e.*, a listing). Thus, it is not obvious that the claims are directed to an apparatus (as claimed) because it is not known what structural components (hardware, software) of "a computing device" are specifically required by the claims; therefore, the system is not interpreted to be a device. Thus, the claims read on a computer program. Computer programs, *per se*, are not statutory. A computer program is not a physical "thing." It is neither a computer component nor a statutory process, as it is not "act" being performed. "Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized." *See* MPEP § 2106.

Claim Rejections - 35 USC § 112

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

a) The breadth of the claims;
b) The nature of the invention;
c) The state of the prior art;
d) The level of one of ordinary skill;
e) The level of predictability in the art;
f) The amount of direction provided by the inventor;
g) The existing of working examples; and
h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

a) The claims are broad because they are drawn to a method for guiding selection of a therapeutic treatment regimen comprising steps of providing information about methylation of DNA of a patient and generating a ranked list of diseases based on the methylation and knowledge base based on general expert rules for evaluating and selecting a type of disease based on methylation status of DNA of a patient. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to generate general or common "expert rules" for analysis and selection of unidentified diseases wherein the disease is associated with a methylation status. The instant specification further does not provide general parameters of the selection of a disease, *e.g.*, whether the selection must be a perfect match or if not, than the threshold for the selection are not clear or directed. The instant specification also does not provide how to generate a ranking list of diseases based on a methylation status nor any criteria for ranking. Without knowing general "expert rules" for evaluating a generic disease, how to select a disease based on a common process, and what common criteria to use for ranking diseases, the selection of a treatment regimen would require undue experimentation.

b) The invention is drawn to a method for guiding selection of a therapeutic treatment regimen.

c), e) Prior art analysis shows that identifying a disease based on a methylation pattern is very complicated and still not well defined, as is identifying therapeutics and treatment regimens for various diseases and stages of a disease. *See* Szyf, *Pharmacolo. Ther.*, 70(1):1-37 (1996). For example, there is a fifty percent chance to correctly determine, based on methylation data, that a patient has myelodysplastic syndrome (MDS). According to Uchida, *Blood*, 90(4):1403-09 (1997), hypermethylation of the 5'OpG island of p15INK4B gene occurs frequently in patients

with MDS (16/32 [50%]) (p. 1403). Nosaka discloses that CDKN2A gene was methylated in 47% of fresh tumor cells isolated from patients with acute ATL, 73% in patients with lymphoma-type ATL, and 17% in patients with malignant chronic and smoldering ATL. Among fresh ATL samples with methylation, methylation in the exon without promoter region was detected in 7 of 24 cases. See Nosaka, *Cancer Res.*, 60(4):1043-8 (Feb. 15, 2000). Ben-Yehuda discloses that of the 148 samples drawn from patients with leukemia (CML) in the chronical phase, 74% were not methylated. Ben-Yehuda, *Blood*, 90(12):4918-23 (1997). Therefore, a method that is based on data that is at most fifty percent accurate would require sufficient guidance and directions in forming "expert rules" to enable a person of ordinary skill in the art to make and use the invention without requiring undue experimentation.

Further, Nosaka discloses using diagnostic criteria that are more than just methylation status. Shymoyama discloses that there are four clinical subtypes of adult T-cell leukemia-lymphoma and each subtype has its unique diagnostic criteria. Shymoyama, *Br. J. Haematol.*, 79(3):428-37 (1991). The different sets of criteria are critical for T-cell leukemia-lymphoma diagnosis. Ben-Yehuda discloses methylation may be used, *in combination with other parameters,* as an aid for deciding on the appropriate mode of treatment and for monitoring time point and other signs of disease progression (CML). The instant specification does not provide any parameters with which a common process of selecting a disease and ranking listing of diseases based on information about methylation is to be practiced. Further, the specification does not provide any parameters within which the diagnostic criteria to each disease are to be used in terms of ranking the disease.

d) The skill of those in the art of molecular biology and bioinformatics is high.

f) The specification does not provide working examples wherein any parameters with which a common process of selecting a disease and ranking listing of diseases based on information about methylation is to be practiced. Further, the specification does not provide any parameters within which the diagnostic criteria to each disease are to be used in terms of ranking the disease.

h) In order to practice the claimed invention, one skilled in the art must randomly select a common expert rule for all diseases and must guess which parameters to use for selecting and ranking diseases. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art showing that the diagnosis of different stages, traits, or diseases requires using complex criteria and expert rules, the specification fails to teach one skilled in the art how to use the claimed method for

Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-50 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is directed to a method for selecting a treatment regimen comprising providing information about methylation to a computing device comprising a first knowledge base

comprising information about methylation of known disease and a second knowledge base comprising expert rules for evaluating and selecting a type of disease. It is not clear whether provided information comprises a first and second knowledge base OR a computer device. The examiner interprets the claim so that a computer device comprises a first and second knowledge base (see, for example claim 28 for support of the instant interpretation). It is further not clear what further limitation of the method step of providing is intended by reciting elements of a computing device (*i.e.*, a first and second knowledge). Specifically, it is not clear whether the applicants intended to limit the method step OR the data (provided information). If the latter, then it is not clear what further limitation of data (information) used in the claimed method is intended by reciting elements composing a computer device. If the former, then the claims should be rewritten using active, positive claim language. As the intended limitation is not clear, claims 1-13 are indefinite.

Claims 1 and 28 are directed to a method and system for selecting a treatment of a patient wish a disease. Claim 14 is directed to a method for treatment of a patient. However, the claims do not recite any step of selecting a treatment nor actual treatment of a patient and only recite providing information and generating a ranked list of diseases. Therefore, the relationship of the preamble and the method steps is not clear and whether the preamble is intended to limit the instant method and a system. It is noted that dependent claims 2-5, 9, 12, 16-19, 23-24, 26, and 29-31 do recite treatment regimens for a patient. As the intended limitation is not clear, claims 1, 6-13, 14-15, 20-22, 25, 27, and 32-39 are indefinite.

Claims 2, 4, 16, and 18 recite the "method according to [a parental claim], further comprising" a third, fourth, and/or fifth knowledge base." It is not clear where these limitations

fit within the parental claims, *e.g.*, whether a third, fourth, and/or fifth knowledge base is a further limitation of the method steps OR is a component of a computing device recited in the parental claims. Similarly, claims 29-30 the "system according to [a parental claim], further comprising" a third, fourth, and/or fifth knowledge base." It is not clear where these limitations fit within the parental claims, e.g., whether the third, fourth, and/or fifth knowledge base is an element of the system (similar to elements A, B, and C) OR a computing device (similar to a first and second knowledge base). As the intended limitation is not clear, claims 2-5, 9, 16-19, 23-24, and 29-30 are indefinite.

Claims 4 and 18 recite the limitation "said ranked listing." The antecedent basis of the limitation is not clear because claims 4 depends from claims 1 and 2and claim 18 depends from claims 14 and 16 that recite "ranked listing of diseases" and "ranked listing of available therapeutic treatment regimens." As the intended limitation is not clear, claims 4, 9, 18, and 23 are indefinite.

Claims 4, 18, 30, and 40 recite the limitation "advisory information useful for the treatment of a patient." The limitation makes the claims vague and indefinite because metes and bounds of the claims is not clear, *i.e.*, criteria of "usefulness" of information is not clear. As the intended limitation is not clear, claims 4, 9, 18, 23, and 40-50 are indefinite.

Claims 5 and 19 recite "entering a user-defined ... regimen." It is not clear where and by whom the regimens is being entered. As the intended limitation is not clear, claims 9 and 19 are indefinite.

Claims 9 and 23 recite the limitation "warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and information clinically useful to implement a corresponding therapeutic treatment regimen." It is not clear to what "a corresponding regimen" corresponds, e.g., to a contraindicated drug, a patient methylation status, *etc.*

It is further unclear whether "a corresponding treatment regimen" recited in lines 2 and 3 are intended to be the same or different regimens.

The limitation "clinically useful to implement" makes the claim vague and indefinite because metes and bounds of the claim is not clear, *i.e.*, criteria of "usefulness" is unclear.

As the intended limitation is not clear, claims 9 and 23 are indefinite.

Claims 10 and 36 recite the limitation "a sixth knowledge base comprising ... said advisory information ... extracted from said sixth knowledge base." The antecedent basis of the limitation "said advisory information" is not clear because claims 1 and 28 do not recite any advisory information.

The limitation "a sixth base" makes claims vague and indefinite because claims 10 and 36 depend from claims 1 and 28, respectively, that only recite a first and second knowledge base, but do not recite a third, forth, and fifth base. Similar, claim 30 recites "a fifth knowledge base." Claim 30 depends from claim 28 which only recites a first and second knowledge base. It seems that in the claims some essential steps/limitations are omitted.

As the intended limitation is not clear, claims 10, 30, and 36 are indefinite.

Claims 12, 26, and 38 recite the limitation "drug dosage information is ... adjusted, if necessary, depending upon the patient information." The limitation makes the claims vague and indefinite because it is not clear what for drug dosage information is adjusted and what criteria of adjusting are intended. As the intended limitation is not clear, claims 12, 26, and 38 are indefinite.

Claim 13 recites step (G) for accessing information for treatment regimens from a drug reference source. The relationship of this step to the steps of (A) providing information about the methylation and (B) generating a ranked listing of diseases recite in claim 1 is not clear. Specifically, it is not clear where the "accessing" step fits within the method recited in claim 1. Also, claim 1 only recites steps A and B, while claim 13 recites step G. It seems that steps C-F are missing from claim 13. As the intended limitation is not clear, claim 13 is indefinite.

Claim 14 recites the limitation "providing data about the methylation ... thereby creating a first knowledge base, ... a second knowledge base, ... a third knowledge base." It is not clear whether "thereby creating" is intended to be an active, positive method step, or merely an intended use of the method. It is further unclear whether it is intended to *provide* the methylation status (that creates only a first data) and second and third knowledge bases OR *provide* the methylation status and *create* a first, second, and third knowledge base. As the intended limitation is not clear, claims 14-27 are indefinite.

Claim 27 recites step (J) for accessing information for treatment regimens from a drug reference source. The relationship of this step to the steps A-D of parental claim 14 is not clear. Specifically, it is not clear where the "accessing" step fits within the method recited in claim 14.

Also, claim 14 only recites steps A-D, while claim 27 recites step J. It seems that steps E-I are missing from claim 27. As the intended limitation is not clear, claim 27 is indefinite.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-50 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 4-16, 19-20, 23-34, 37-48, and 51-60 of copending Application No. 10/857,105. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marina Miller
Examiner
Art Unit 1631

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
1/18/07

MM